U.S. Serial No.: 10/671,326

Page 2 of 53

The following list of claims replaces all prior versions and lists cf claims in the application:

## Listing of Claims:

1. (Currently amended) A compound having the formula:

$$\begin{array}{c|c}
G & A & A \\
\hline
A & Z & B_p - (CH_2)_q - D - E \\
\hline
A & Z & B_p - (CH_2)_q - D - E
\end{array}$$

or a pharmaceutically acceptable salt, ester, or prodrug thereof, wherein

A<sub>5</sub> at each occurrence, independently is carbon, earbonyl, or nitre gen, provided at least one A is earbon;

Z is carbon, nitrogen, oxygen, or sulfur;

B is selected from the group consisting of O, NR<sup>2</sup>, S(O)<sub>r</sub>, C=O, C=S, and C=NOR<sup>3</sup>,

p is 0-or 1;

q, at each occurrence, independently is 0 or 1;

r is 0, 1, or 2;

R<sup>2</sup>, at each occurrence, independently is selected from the group consisting of:

a) hydrogen, b) S(O)<sub>r</sub>R<sup>4</sup>, c) formyl, d) C<sub>1-8</sub> alkyl, e) C<sub>2-8</sub> alkenyl, f) C<sub>2-8</sub>
alkynyl, g) C<sub>1-8</sub> alkoxy, h) C<sub>1-8</sub> alkylthio, i) C<sub>1-8</sub> acyl, j) saturated,
unsaturated, or aromatic C<sub>3-8</sub> carbocycle, and k) saturated unsaturated, or
aromatic 5-10 membered heterocycle containing one or more heteroatoms
selected from the group consisting of nitrogen, oxygen, at d sulfur,

 Amendment U.S. Serial No.: 10/671,326 Page 3 of 53

 $NO_2$ ,  $-NR^3R^3$ ,  $-OR^3$ ,  $-S(O)_rR^4$ ,  $-S(O)_rNR^3R^3$ ,  $-C(C)R^3$ ,  $-C(O)OR^3$ ,  $-OC(O)R^3$ ,  $-C(O)NR^3R^3$ , and  $-OC(O)NR^3R^3$ ;

alternatively, two R<sup>2</sup> groups, taken together with the atom to which they are bonded, form i) 5-8 membered saturated or unsaturated carbocycle, or ii) 5-8 membered saturated or unsaturated heterocycle containing one or more atoms selected from the group consisting of nitrogen, oxygen, and sulfur,

wherein i) – ii) optionally is substituted with one or more moieties selected from the group consisting of carbonyl, F, Cl, Br, I, CN, NO<sub>2</sub>, -NR<sup>3</sup>R<sup>3</sup>, -OR<sup>3</sup>, -S(O)<sub>1</sub>R<sup>4</sup>, -S(O)<sub>1</sub>NR<sup>3</sup>R<sup>3</sup>, -C(O)R<sup>3</sup>, -C(O)OR<sup>3</sup>, -OC(O)NR<sup>3</sup>R<sup>3</sup>, -OC(O)NR<sup>3</sup>R<sup>3</sup>, Cl<sub>1-6</sub> acyl, aryl, substituted aryl, heteroaryl, and substituted heteroaryl;

R<sup>3</sup>, at each occurrence, independently is selected from the group consisting of:

a) hydrogen, b) C<sub>1-8</sub> alkyl, c) C<sub>2-8</sub> alkenyl, d) C<sub>2-8</sub> alkynyl, e) C<sub>1-8</sub> acyl,

f) saturated, unsaturated, or aromatic C<sub>3-8</sub> carbocycle, and g) saturated,
unsaturated, or aromatic 5-10 membered heterocycle containing one or
more heteroatoms selected from the group consisting of nitrogen, oxygen,
and sulfur,

wherein any of b) – h) optionally is substituted with one or more moieties selected from the group consisting of carbonyl, F, Cl, Br, I, CN, NO<sub>2</sub>, -NR<sup>6</sup>R<sup>6</sup>, -OR<sup>6</sup>, -S(O)<sub>r</sub>R<sup>6</sup>, -S(O)<sub>r</sub>NR<sup>6</sup>R<sup>1</sup>, -C(O)R<sup>6</sup>, -C(O)OR<sup>6</sup>, -OC(O)NR<sup>6</sup>R<sup>6</sup>, -OC(O)NR<sup>6</sup>F.<sup>6</sup>, C<sub>1-6</sub> acyl, aryl, substituted aryl, heteroaryl, and substituted heteroaryl;

alternatively, two R<sup>3</sup> groups, taken together with the atom to which they are bonded, form i) a 5-7 membered saturated or unsaturated carbocycle, or ii) a 5-7 membered saturated or unsaturated heterocycle containing one or more a oms selected from the group consisting of nitrogen, oxygen, and sulfur,

wherein i) - ii) optionally is substituted with one or more moieties selected from the group consisting of carbonyl, F, Cl, Br, I, CN,  $NO_2$ ,  $-NR^6R^6$ ,  $-OR^6$ ,  $-S(O)_rR^6$ ,  $-S(O)_rR^6$ ,  $-C(O)R^6$ ,  $-C(O)OR^6$ ,  $-OC(O)R^6$ ,

Amendment U.S. Serial No.: 10/671,326 Page 4 of 53

-C(O)NR<sup>6</sup>R<sup>6</sup>, -OC(O)NR<sup>6</sup>R<sup>6</sup>,  $C_{1-6}$  acyl, aryl, substituted aryl, heteroaryl, and substituted heteroaryl;

R<sup>4</sup> is selected from the group consisting of:

a) hydrogen, b) -NR<sup>3</sup>R<sup>3</sup>, c) -NR<sup>3</sup>OR<sup>3</sup>, d) -NR<sup>3</sup>NR<sup>3</sup>R<sup>3</sup> e) -NHC(O)R<sup>3</sup>, f) -C(O)NR<sup>3</sup>R<sup>3</sup>, g) -N<sub>3</sub>, h) C<sub>1-8</sub> alkyl, i) C<sub>2-8</sub> alkenyl, j) C<sub>1-8</sub> alkynyl, k) saturated, unsaturated, or aromatic C<sub>3-8</sub> carbocycle, and l) saturated, unsaturated, or aromatic 5-10 membered heterocycle con aining one or more heteroatoms selected from the group consisting of r itrogen, oxygen, and sulfur,

wherein any of h) – l) optionally is substituted with one or more moieties selected from the group consisting of carbonyl, F, Cl, Br, I, CN, NO<sub>2</sub>, -NR<sup>3</sup>R<sup>3</sup>, -OR<sup>3</sup>, -SR<sup>3</sup>, -S(O)<sub>r</sub>R<sup>5</sup>, -S(O)<sub>l</sub>NR<sup>3</sup>R<sup>3</sup>, -C(O)R<sup>3</sup>, -C(O)OR<sup>3</sup>, -OC(O)NR<sup>3</sup>R<sup>3</sup>, -OC(O)NR<sup>3</sup>R<sup>3</sup>, -OC(O)NR<sup>3</sup>R<sup>3</sup>, Cl<sub>-6</sub> alkyl, Cl<sub>-6</sub> alkenyl, Cl<sub>-6</sub> alkynyl, Cl<sub>-6</sub> acyl, aryl, substituted aryl, heteroaryl, and substituted heteroaryl;

R<sup>5</sup> is selected from the group consisting of:

a) hydrogen, b) -NR<sup>3</sup>R<sup>3</sup>, c) -NR<sup>3</sup>OR<sup>3</sup>, d) -NR<sup>3</sup>NR<sup>3</sup>R<sup>3</sup> e) NHC(O)R<sup>3</sup>, f) -C(O)NR<sup>3</sup>R<sup>3</sup>, g) -N<sub>3</sub>, h) C<sub>1-8</sub> alkyl, i) C<sub>2-8</sub> alkenyl, j) C<sub>2-8</sub> alkynyl, k) saturated, unsaturated, or aromatic C<sub>3-8</sub> carbocycle, and l) saturated, unsaturated, or aromatic 5-10 membered heterocycle containing one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

wherein any of h) – l) optionally is substituted wit 1 one or more moieties selected from the group consisting of F, Cl, Br, I, CN,  $NO_2$ ,  $-NR^3R^3$ ,  $-OR^3$ ,  $-SR^3$ -C(O) $R^3$ ,  $-C(O)OR^3$ ,  $-OC(O)R^3$ ,  $-C(O)NR^3R^3$ ,  $-OC(O)NR^3R^3$ ,  $C_{1-6}$  alkyl,  $C_{1-6}$  alker yl,  $C_{1-6}$  alkynyl,  $C_{1-6}$  acyl, aryl, substituted aryl, heteroaryl, and substituted heteroaryl:

R<sup>6</sup>, at each occurrence, independently is selected from the group consisting of:

U.S. Serial No.: 10/671,326

Page 5 of 53

hydrogen,  $C_{1-6}$  alkyl,  $C_{1-6}$  alkenyl,  $C_{1-6}$  alkynyl,  $C_{1-6}$  acyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl;

alternatively, two R<sup>6</sup> groups taken together are -(CH<sub>2</sub>)<sub>s</sub>-,

wherein s is 1, 2, 3, 4, or 5;

D-E is selected from the group consisting of:

E is selected from the group consisting of:

a)

b)

c)

d) 5-10 membered saturated, unsaturated, or aromatic heterocycle containing one or more heteroatoms selected from the group consisting of nitrogen, exygen, and sulfur, and optionally substituted with one or more R<sup>13</sup> groups; and

U.S. Serial No.: 10/671,326

Page 6 of 53

e)  $C_{5-10}$  saturated, unsaturated, or aromatic carbocycle, opticnally substituted with one or more  $R^{13}$  groups;

- f) C<sub>1.8</sub> alkyl,
- g) -- C<sub>2-8</sub> alkenyl,
- h) C<sub>3-8</sub> alkynyl,
- i) CLe-alkoxy,
- j) -- C<sub>1.8</sub> alkylthio,
- k)  $C_{1.8}$  acyl,
- l) S(O), R<sup>5</sup>; and
- m) hydrogen,

wherein any of f) - k) optionally is substituted with

- i) one or more R<sup>13</sup>-groups;
- ii) 5-6 membered saturated, unsaturated, or aromatic heterocycle containing one or more heteroatoms solected from the group consisting of nitrogen, oxygen, and sulfur, and optionally substituted with one or more R<sup>13</sup> groups; or
- iii) C<sub>5-10</sub> saturated, unsaturated, or aromatic carbocycle, optionally substituted with one or more R<sup>13</sup> groups;

R<sup>7</sup> is selected from the group consisting of:

- a) hydrogen, b) carbonyl, c) formyl, d) F, e) Cl, f) Br, g) I, h) CN, i) NO2,
- j)  $OR^3$ , k)  $-S(O)_iR^5$ , l)  $-S(O)_iN=R^2$ , m)  $-C(O)R^2$ , n)  $-C(O)\cap R^3$ , o)
- $-OC(O)R^2$ , p)  $-C(O)NR^2R^2$ , q)  $-OC(O)NR^2R^2$ , r)  $-C(=NR^{12})R^2$ , s) -
- $C(R^2)(R^2)OR^3$ , t)  $-C(R^2)(R^2)OC(O)R^2$ , u)  $-C(R^2)(OR^3)(CH_2)NR^2R^2$ , v)
- $-NR^2R^2$ , w)  $-NR^2OR^3$ , x)  $-N(R^2)C(O)R^2$ , y)  $-N(R^2)C(O)O(R^3$ , z)
- -N(R2)C(O)NR2R2, aa) -N(R2)S(O),R5, bb) -C(OR6)(OR6)R2,
- cc)  $-C(R^2)(R^3)NR^2R^2$ , dd)  $-C(R^2)(R^3)NR^2R^{12}$ , ee)  $=NR^{12}$ , ff)  $-C(S)NR^2R^2$ ,
- gg)  $-N(R^2)C(S)R^2$ , hh)  $-OC(S)NR^2R^2$ , ii)  $-N(R^2)C(S)OR^3$ ,
- jj) -N(R<sup>2</sup>)C(S)NR<sup>2</sup>R<sup>2</sup>, kk) -SC(O)R<sup>2</sup>, ll)  $C_{1-8}$  alkyl, mm)  $C_{2-8}$  alkenyl,
- nn)  $C_{2-8}$  alkynyl, oo)  $C_{1-8}$  alkoxy, pp)  $C_{1-8}$  alkylthio, qq)  $C_{-8}$  acyl, rr)
- saturated, unsaturated, or aromatic C<sub>5-10</sub> carbocycle, and s:) saturated,

U.S. Serial No.: 10/671,326

Page 7 of 53

unsaturated, or aromatic 5-10 membered heterocycle con aining one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

wherein any of ll) – ss) optionally is substituted with one or more moieties selected from the group consisting of:

carbonyl; formyl; F; Cl; Br; I; CN; NO<sub>2</sub>; OR<sup>3</sup>; -S<sub>1</sub>O)<sub>r</sub>R<sup>5</sup>;
-S(O)<sub>r</sub>N=R<sup>2</sup>, -C(O)R<sup>2</sup>; -C(O)OR<sup>3</sup>; -OC(O)R<sup>2</sup>; -C(O)NR<sup>2</sup>R<sup>2</sup>;
-OC(O)NR<sup>2</sup>R<sup>2</sup>; -C(=NR<sup>10</sup>)R<sup>2</sup>; -C(R<sup>2</sup>)(R<sup>2</sup>)OR<sup>3</sup>;
-C(R<sup>2</sup>)(R<sup>2</sup>)OC(O)R<sup>2</sup>; -C(R<sup>2</sup>)(OR<sup>3</sup>)(CH<sub>2</sub>)<sub>r</sub>NR<sup>2</sup>R<sup>2</sup>; ·NR<sup>2</sup>R<sup>2</sup>;
-NR<sup>2</sup>OR<sup>3</sup>; -NR<sup>2</sup>C(O)R<sup>2</sup>; -NR<sup>2</sup>C(O)OR<sup>3</sup>; -NR<sup>2</sup>C(O)NR<sup>2</sup>R<sup>2</sup>;
-NR<sup>2</sup>S(O)<sub>r</sub>R<sup>5</sup>; -C(OR<sup>6</sup>)(OR<sup>6</sup>)R<sup>2</sup>; -C(R<sup>2</sup>)(R<sup>3</sup>)NR<sup>2</sup>R<sup>2</sup>;
-C(R<sup>2</sup>)(R<sup>3</sup>)NR<sup>2</sup>R<sup>12</sup>; =NR<sup>12</sup>; -C(S)NR<sup>2</sup>R<sup>2</sup>; -NR<sup>2</sup>C(S)R<sup>2</sup>;
-OC(S)NR<sup>2</sup>R<sup>2</sup>; -NR<sup>2</sup>C(S)OR<sup>3</sup>; -NR<sup>2</sup>C(S)NR<sup>2</sup>R<sup>2</sup>; ·SC(O)R<sup>2</sup>;
C<sub>2-5</sub> alkenyl; C<sub>2-5</sub> alkynyl; C<sub>1-8</sub> alkoxy; C<sub>1-8</sub> alkylthio; C<sub>1-8</sub> acyl; saturated, unsaturated, or aromatic C<sub>5-10</sub> carbocyc e, optionally substituted with one or more R<sup>8</sup> groups; and saturated, unsaturated, or aromatic 5-10 membered heterocycle containing one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, and optionally substituted wit 1 one or more R<sup>8</sup> groups;

R<sup>8</sup> is selected from the group consisting of:

hydrogen; F; Cl; Br; I; CN; NO<sub>2</sub>; OR<sup>6</sup>; aryl; substituted a ryl; heteroaryl; substituted heteroaryl; and C<sub>1-6</sub> alkyl, optionally substituted with one or more moieties selected from the group consisting of aryl, substituted aryl, heteroaryl, substituted heteroaryl, F, Cl, Br, I, CN, NO<sub>2</sub>, and OR<sup>6</sup>;

alternatively, R<sup>7</sup> and R<sup>8</sup> taken together are -O(CH<sub>2</sub>)<sub>r</sub>O-;

R<sup>9</sup>, at each occurrence, independently is selected from the group consisting of: hydrogen, F, Cl, Br, I, CN, OR<sup>3</sup>, NO<sub>2</sub>, -NR<sup>2</sup>R<sup>2</sup>, C<sub>1-6</sub> alkyl C<sub>1-6</sub> acyl, and C<sub>1-6</sub> alkoxy;

R<sup>10</sup> is selected from the group consisting of:

U.S. Serial No.: 10/671,326

Page 8 of 53

a) saturated, unsaturated, or aromatic C<sub>5-10</sub> carbocycle, b) saturated, unsaturated, or aromatic 5-10 membered heterocycle con aining one or more heteroatoms selected from the group consisting of r itrogen, oxygen, and sulfur, c) -X-C<sub>1-6</sub> alkyl-saturated, unsaturated, or aromatic 5-10 membered heterocycle containing one or more heteroator is selected from the group consisting of nitrogen, oxygen, and sulfur, d) saturated, unsaturated, or aromatic 10-membered bicyclic ring system optionally containing one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, e) saturated, unsaturated, or aromatic 13-membered tricyclic ring system optionally containing one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, and f) R<sup>9</sup>,

wherein

any of a) - e) optionally is substituted with one or more R<sup>13</sup> groups, and

X is O or NR<sup>3</sup>;

alternatively, R<sup>10</sup> and one R<sup>9</sup> group, taken together with the atom; to which they are bonded, form a 5-7 membered saturated or unsaturated carbocycle, oritionally substituted with one or more R<sup>13</sup> groups; or a 5-7 membered saturated or unsaturated heterocycle containing one or more atoms selected from the group consisting of nitrogen, oxygen, and sulfur, and optionally substituted with one or more R<sup>13</sup> groups:

R<sup>11</sup> at each occurrence, independently is selected from the group consisting of: hydrogen; an electron-withdrawing group; aryl; substituted aryl; heteroaryl; substituted heteroaryl; and C<sub>1-6</sub> alkyl, optionally substituted with F, Cl, or Br;

alternatively, any R<sup>11</sup> and R<sup>8</sup>, taken together with the atoms to which they are bonded, form a 5-7 membered saturated or unsaturated carbocycle, optio ally substituted with one or more R<sup>13</sup> groups; or a 5-7 membered saturated or unsaturated heterocycle containing one or more atoms selected from the group consisting of nitrogen, oxygen, and sulfur, and optionally substituted with one or more R<sup>13</sup> groups;

Amendment U.S. Serial No.: 10/671,326 Page 9 of 53

> R<sup>12</sup> is selected from the group consisting of:  $-NR^2R^2$ ,  $-OR^3$ ,  $-OC(O)R^2$ ,  $-OC(O)OR^3$ ,  $-NR^2C(O)R^2$ ,  $-NR^2C(O)NR^2R^2$ ,

-NR<sup>2</sup>C(S)NR<sup>2</sup>R<sup>2</sup>, and -NR<sup>2</sup>C(=NR<sup>2</sup>)NR<sup>2</sup>R<sup>2</sup>:

R<sup>13</sup>, at each occurrence, independently is selected from the group consisting of: a) hydrogen, b) carbonyl, c) formyl d) F, e) Cl, f) Br, g) I, h) CN, i) NO2, j)  $OR^3$ , k)  $-S(O)_rR^5$ , l)  $-S(O)_rN=R^3$ , m)  $-C(O)R^2$ , n)  $-C(O)OR^3$ , o)  $-OC(O)R^2$ . p)  $-C(O)NR^2R^2$ , q)  $-OC(O)NR^2R^2$ , r)  $-C(=NR^{12})R^2$ , s)  $-C(R^2)(R^2)OR^3$ . t)  $-C(R^2)(R^2)OC(O)R^2$ , u)  $-C(R^2)(OR^3)(CH_2)NR^2R^2$ , v)  $-NR^2R^2$ , w)  $-NR^2OR^3$ , x)  $-N(R^2)C(O)R^2$ , y)  $-N(R^2)C(O)OR^3$ , z)  $-N(R^2)C(O)NR^2R^2$ , aa)  $-N(R^2)S(O)_{1}R^5$ , bb)  $-C(OR^6)(OR^6)R^2$ , cc)  $-C(R^2)(R^3)NR^2iR^2$ , dd)  $-C(R^2)(R^3)NR^2R^{12}$ , ee) =  $NR^{12}$ , ff)  $-C(S)NR^2R^2$ , gg)  $-N(R^3)C(S)R^2$ , hh)  $-OC(S)NR^2R^2$ , ii)  $-N(R^2)C(S)OR^3$ , ii)  $-N(R^2)C(S)NR^2R^2$ , kk)  $-SC(O)R^2$ . ll) C<sub>1-8</sub> alkyl, mm) C<sub>2-8</sub> alkenyl, nn) C<sub>2-8</sub> alkynyl, oo) C<sub>1-8</sub> alkoxy, pp) C<sub>1-8</sub> alkylthio, qq) C<sub>1-8</sub> acyl, rr) saturated, unsaturated or aromatic C<sub>5</sub> 10 carbocycle, ss) saturated, unsaturated, or aromatic 5-10 membered heterocycle containing one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, tt) saturated, unsaturated, or aromatic 10-membered bicyclic ring system optionally containing one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, and uu) saturated, unsaturated, or aromatic 13-membered tricyclic ring system optionally containing one or more heteroatoms

wherein any of ll) - uu) optionally is substituted with one or more moieties selected from the group consisting of:

selected from the group consisting of nitrogen, oxygen, and sulfur,

carbonyl; formyl; F; Cl; Br; I; CN; NO<sub>2</sub>; OR<sup>3</sup>; -S(O)<sub>2</sub>R<sup>5</sup>;  $-S(O)_{r}N=R^{2}$ ,  $-C(O)R^{2}$ ;  $-C(O)OR^{3}$ ;  $-OC(O)R^{2}$ ;  $-C(O)NR^{2}R^{2}$ ;  $-OC(O)NR^2R^2$ ;  $-C(=NR^{12})R^2$ ;  $-C(R^2)(R^2)CR^3$ ;  $-C(R^2)(R^2)OC(O)R^2$ ;  $-C(R^2)(OR^3)(CH_2)NR^2R^2$ ;  $-NR^2R^2$ ;  $-NR^2OR^3$ ;  $-NR^2C(O)R^2$ ;  $-NR^2C(O)OR^3$ ;  $-NR^2C(O)NR^2R^2$ ;  $-NR^2S(O)_*R^5$ ;  $-C(OR^6)(OR^6)R^2$ :  $-C(R^2)(R^3)NR^2R^2$ :

Amendment U.S. Serial No.: 10/671,326 Page 10 of 53

> -C(R<sup>2</sup>)(R<sup>3</sup>)NR<sup>2</sup>R<sup>12</sup>; =NR<sup>12</sup>; -C(S)NR<sup>2</sup>R<sup>2</sup>; ·NR<sup>2</sup>C(S)R<sup>2</sup>; -OC(S)NR<sup>2</sup>R<sup>2</sup>; -NR<sup>2</sup>C(S)OR<sup>3</sup>; -NR<sup>2</sup>C(S)NR<sup>2</sup>R<sup>2</sup>; -SC(O)R<sup>2</sup>; C<sub>1-8</sub> alkyl, C<sub>2-8</sub> alkenyl; C<sub>2-8</sub> alkynyl; C<sub>1-8</sub> alkoxy; C<sub>1-8</sub> alkylthio; C<sub>1-8</sub> acyl; saturated, unsaturated or aromatic C<sub>3-10</sub> carbocycle optionally substituted with one or more R<sup>7</sup> groups; and saturated, unsaturated, or aromatic 3-10 membered heterocycle containing one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, and substituted with one or more R<sup>7</sup> groups;

G is selected from the group consisting of:

a) C<sub>1-4</sub> alkyl, b) C<sub>5-8</sub> alkyl, c) C<sub>2-8</sub> alkenyl, d) C<sub>2-8</sub> alkynyl. e) C<sub>1-8</sub> alkoxy, f) C<sub>1-8</sub> alkylthio, g) saturated, unsaturated, or aromatic C<sub>5-10</sub> carbocycle, h) saturated, unsaturated, or aromatic 5-10 membered heterc cycle containing one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

$$\frac{i}{\xi} \xrightarrow{Q} (CH_{2}) \xrightarrow{Q} (CH_{2}) \xrightarrow{R^{14}} Q \xrightarrow{Q} (CH_{2}) \xrightarrow{Q} Q \xrightarrow{Q} \frac{1}{\xi}$$

$$\frac{\xi}{\xi} \xrightarrow{Q} (CH_{2}) \xrightarrow{Q} (CH_{2}) \xrightarrow{Q} (CH_{2}) \xrightarrow{Q} Q \xrightarrow{Q} \frac{1}{\xi}$$

$$\frac{\xi}{\xi} \xrightarrow{Q} (CH_{2}) \xrightarrow{Q} CH = CH \xrightarrow{Q} Q \xrightarrow{Q} Q \xrightarrow{Q} Q \xrightarrow{Q} Q \xrightarrow{Q} Q$$

$$\frac{\xi}{\xi} \xrightarrow{Q} (CH_{2}) \xrightarrow{Q} CH = CH \xrightarrow{Q} Q \xrightarrow{Q} Q \xrightarrow{Q} Q$$

$$\frac{\xi}{\xi} \xrightarrow{Q} (CH_{2}) \xrightarrow{Q} CH = CH \xrightarrow{Q} Q \xrightarrow{Q} Q$$

U.S. Serial No.: 10/671,326

Page 11 of 53

-C(R2)(OR3)(CH2); NR2R2; NR2R2; NF:2OR3; -NR2C(O)R2; NR2C(O)OR3; NR2C(O); IR2R2;

-OC(S)NR2R2; -NR2C(S)OR3; -NR2C(S): VR2R2;

-NR2S(O)rR5; -C(OR6)(OR6)R2; -C(R2)(R3)NR2R2;

-C(R2)(R3)NR2R12; -NR12; -C(S)NR2R'; -NR2C(S)R2;

-SC(O)R2; C2-5 alkonyl; C2-5 alkynyl; C1-8 alkoxy; C1-8 alkylthio; C1-8 acyl; saturated, unsaturated; or aromatic C5-

U.S. Serial No.: 10/671,326

Page 12 of 53

10 carbocycle, optionally substituted with one or more R13 groups; and saturated, unsaturated, or aromatic 5-10 membered heterocycle containing one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, and optionally substituted with one or more R13 groups;

t, at each occurrence, independently is 0, 1, 2, or 3;  $\frac{1}{2}$  v is 0, 1, 2, 3, 4, 5, or 6;

R<sup>14</sup> is selected from the group consisting of:

- a) hydrogen, b)  $C_{1-6}$ -alkyl, c)  $C_{2-6}$  alkenyl, d)  $C_{2-6}$  alkynyl, e)  $-C(O)-R^3$ ,
- f) -C(O)-C<sub>1-6</sub> alkyl-R<sup>3</sup>, g) -C(O)-C<sub>2-6</sub> alkenyl-R<sup>3</sup>, h) -C(O) -C<sub>2-6</sub> alkynyl-R<sup>3</sup>,
- i)  $-C_{1-6}$  alkyl-J-R<sup>3</sup>, j)  $-C_{2-6}$  alkenyl-J-R<sup>3</sup>; and k)  $-C_{2-6}$  alkynyl-J-R<sup>3</sup>; wherein
  - (i) any of b) d) optionally is substituted with one or more substituents selected from the group consisting of:
     F, Cl, Br, I, aryl, substituted aryl, heteroaryl, substituted heteroaryl, -OR<sup>3</sup>, -O-C<sub>1-6</sub> alkyl-R<sup>2</sup>, -O-C<sub>2-6</sub> alkenyl-R<sup>2</sup>, -O-C<sub>2-6</sub> alkynyl-R<sup>2</sup>, and-NR<sup>2</sup>R<sup>2</sup>; and
  - (ii) J is selected from the group consisting of:

    -OC(O)-, -OC(O)O-, -OC(O)NR<sup>2</sup>-, -C(O)NR<sup>2</sup>-, 
    NR<sup>2</sup>C(O)-, -NR<sup>2</sup>C(O)O-, -NR<sup>2</sup>C(O)NR<sup>2</sup>
    -NR<sup>2</sup>C(NH)NR<sup>2</sup>-, and S(O)-; and

R<sup>15</sup> is selected from the group consisting of:

hydrogen;  $C_{1-10}$  alkyl, optionally substituted with one or more  $R^{13}$  groups;  $C_{1-6}$  acyl, optionally substituted with one or more  $R^{13}$  groups; aryl; substituted aryl; heteroaryl; substituted heteroaryl; arylalkyl; substituted arylalkyl; and a macrolide.

2.-4. (Cancelled)

U.S. Serial No.: 10/671,326

Page 13 of 53

5. (Original) The compound according to claim 4, having the formula:

wherein A, E, and G are as defined in claim 1.

6.-8. (Cancelled)

9. (Original) The compound according to claim 1, wherein 3 has the formula:

wherein R<sup>9</sup> and R<sup>10</sup>, at each occurrence, are as defined in claim 1.

10. (Original) The compound according to claim 1, wherein E has the formula:

wherein R<sup>10</sup> is as defined in claim 1.

11. (Original) The compound according to claim 9, wherein R<sup>10</sup> has the formula:

wherein

U.S. Serial No.: 10/671,326

Page 14 of 53

K is selected from the group consisting of O,  $NR^2$ , and S  $O_{r}$ , and x is 0, 1, 2, or 3.

- 12. (Original) The compound according to claim 11, wherein K is oxygen.
- 13. (Previously presented) The compound according to claim 11, wherein x is 1.
- 14. -17 (Cancelled)
- 18. (Original) The compound according to claim 1, wherein G has the formula:

$$\frac{\xi \left( \begin{array}{c} O \\ Q \\ \end{array} \right) \left( CH_2 \right)_t \left( \begin{array}{c} O \\ Q \\ \end{array} \right) \left( CH_2 \right)_t \left( \begin{array}{c} R^{14} \\ N \end{array} \right) \left( \begin{array}{c} R^{13} \\ N \end{array} \right) \left( \begin{array}$$

and R<sup>15</sup> is a macrolide.

19. (Original) The compound according to claim 1, wherein G has the formula:

$$\frac{5\left(\stackrel{O}{\parallel}\right)\left(\operatorname{CH}_{2}\right)_{t}\left(\stackrel{O}{\parallel}\right)_{q}}{\left(\operatorname{CH}_{2}\right)_{t}\left(\stackrel{O}{\parallel}\right)_{q}}\left(\operatorname{CH}_{2}\right)_{t}\left(\stackrel{O}{\parallel}\right)_{q}}{\left(\operatorname{CH}_{2}\right)_{t}\left(\stackrel{O}{\parallel}\right)_{q}} \stackrel{R^{14}}{\stackrel{R^{13}}{\parallel}}_{N}$$

$$OF^{14}$$

and R15 is a macrolide.

20. (Original) The compound according to claim 1, wherein R<sup>15</sup> is selected from the group consisting of:

U.S. Serial No.: 10/671,326

Page 15 of 53

$$R^{20}$$
  $R^{19}$   $R^{18}$   $R^{18}$   $R^{20}$   $R^{18}$   $R^{20}$   $R$ 

and pharmaceutically acceptable salts, esters and prodrugs thereof, wherein

R<sup>17</sup> is selected from the group consisting of:

hydrogen, hydroxy protecting group,  $R^3$ , and -V-W- $R^{13}$ , wherein

V is -C(O), -C(O)O-, -C(O)NR<sup>2</sup>-, or absent, and W is C<sub>1-6</sub> alkyl, or absent;

alternatively R<sup>17</sup> and R<sup>14</sup>, taken together with the atoms to which they are bonded, form:

Q is selected from the group consisting of:

$$-NR^2CH_2$$
,  $-CH_2$ - $NR^2$ -,  $-C(O)$ -,  $-C(=NR^2)$ -,  $-C(=NOR^3)$ -,  $-C(=N-NR^2R^2)$ -,  $-CH(OR^3)$ -, and  $-CH(NR^2R^2)$ -;

R<sup>18</sup> is selected from the group consisting of:

i) C<sub>1-6</sub> alkyl, ii) C<sub>2-6</sub> alkenyl, and iii) C<sub>2-6</sub> alkynyl;
 wherein any of i) – iii) optionally is substituted with one or more moieties selected from the group consisting of -OR<sup>3</sup>, aryl, substituted aryl, heteroaryl, and substituted heteroaryl;

R<sup>19</sup> is selected from the group consisting of:

a) 
$$-OR^{17}$$
, b)  $C_{1-6}$  alkyl, c)  $C_{2-6}$  alkenyl, d)  $C_{2-6}$  alkynyl, e)  $-NR^2R^2$ , f)  $-C(O)R^3$ , g)  $-C(O)-C_{1-6}$  alkyl- $R^{13}$ , h)  $-C(O)-C_{2-6}$  alkenyl- $R^{3}$ , and i)  $-C(O)-C_{2-6}$  alkynyl- $R^{13}$ .

Amendment U.S. Serial No.: 10/671,326 Page 16 of 53

wherein any of b) - d) optionally is substituted with one or more R<sup>13</sup> groups;

alternatively, R<sup>14</sup> and R<sup>19</sup>, taken together with the atoms to which they are bonded, form:

wherein

L is CH or N, and R<sup>23</sup> is -OR<sup>3</sup>, or R<sup>3</sup>;

 $R^{20}$  is  $-OR^{17}$ :

alternatively, R<sup>19</sup> and R<sup>20</sup>, taken together with the atoms to which they are bonded, form a 5-membered ring by attachment to each other through a linker selected from the group consisting of:

 $-{\rm OC}({\rm R}^2)({\rm R}^2){\rm O-,-OC}({\rm O}){\rm O-,-OC}({\rm O}){\rm NR}^2-,-{\rm NR}^2{\rm C}({\rm O}){\rm O-,-OC}({\rm O}){\rm NOR}^3-,$ 

 $-N(OR^3)C(O)O-, -OC(O)N-NR^2R^2-, -N(NR^2R^2)C(O)O-, -OC(O)CHR^2-, -N(OR^3)C(O)O-, -OC(O)CHR^2-, -N(OR^3)C(O)O-, -OC(O)CHR^2-, -N(OR^3)C(O)O-, -OC(O)CHR^2-, -N(OR^3)C(O)O-, -OC(O)CHR^2-, -N(OR^3)C(O)O-, -OC(O)CHR^3-, -N(OR^3)C(O)O-, -N(OR^3$ 

 $-CHR^2C(O)O-, -OC(S)O-, -OC(S)NR^2-, -NR^2C(S)O-, -OC(S)NOR^3-, -OC(S)O-, -O$ 

-N(OR $^3$ )C(S)O-, -OC(S)N-NR $^2$ R $^2$ -, -N(NR $^2$ R $^2$ )C(S)O-, -OC(S)CHR $^2$ -, and

-CHR<sup>2</sup>C(S)O-;

alternatively, Q, R<sup>19</sup>, and R<sup>20</sup>, taken together with the atoms to which they are bonded, form:

wherein

M is O or NR<sup>2</sup>;

Amendment U.S. Serial No.: 10/671,326

Page 17 of 53

R<sup>21</sup> is selected from the group consisting of:

hydrogen, F, Cl, Br, and C<sub>1-6</sub> alkyl;

 $R^{22}$ , at each occurrence, independently is selected from the group consisting of: hydrogen, -OR<sup>3</sup>, -O-hydroxy protecting group, -O-C<sub>1-6</sub> alkyl-J-R<sup>13</sup>, -O-C<sub>2-6</sub> alkenyl-J-R<sup>13</sup>, -O-C<sub>1-6</sub> alkynyl-J-R<sup>13</sup>, and -NR<sup>2</sup>R<sup>2</sup>;

alternatively, two  $R^{22}$  groups taken together are =0, =N-OR<sup>3</sup>, or =N-NR<sup>2</sup>R<sup>2</sup>; and  $R^2$ ,  $R^3$ ,  $R^{13}$ ,  $R^{14}$ , and J are as described in claim 1.

21. (Original) The compound according to claim 1, wherein G has the formula selected from the group consisting of:

and R<sup>15</sup> has the formula selected from the group consisting of:

U.S. Serial No.: 10/671,326 Page 18 of 53

U.S. Serial No.: 10/671,326

Page 19 of 53

22. (Original) The compound according to claim 1, wherein G has the formula:

wherein n = 1, 2, 3, or 4.

- 23. (Cancelled)
- 24. (Original) The compound according to claim 1, wherein G has the formula:

Amendment U.S. Serial No.: 10/671,326 Page 20 of 53

wherein n = 1, 2, 3, or 4.

## 25. - 26. (Cancelled)

27. (Original) The compound according to claim 26, wherein G has the formula selected from the group consisting of:

U.S. Serial No.: 10/671,326 Page 21 of 53

U.S. Serial No.: 10/671,326

Page 22 of 53

## 28.-29. (Cancelled).

## 30. (Currently amended) A compound having the structure corresponding to any of the structures listed below:

Compound Number	Structure
142	
143	N OH
144	N N N N N N N N N N N N N N N N N N N
145	P NOM OH
146	E N N N OH OH
147	No. No. OH

U.S. Serial No.: 10/671,326 Page 23 of 53

148	DH 3CH b
149	HO DE NOCH
150	HO THE STATE OF TH
151	HO WILL HO WAY
152	HO OH O
153	HO HO HO

U.S. Serial No.: 10/671,326

Page 24 of 53

175	
176	NEN OH ME
177	N N N OME
178	N=N N=N N=N N=N N=N N=N N=N N=N N=N N=N
179	N=N N=N N-OH OH OH OH OH OH

U.S. Serial No.: 10/671,326

Page 25 of 53

180	N=N N=N N=N N=N N=N N=N N=N N=N N=N N=N
181	HO OH OME
182	
183	

U.S. Serial No.: 10/671,326 Page 26 of 53

184	
185	HO H
186	F N N N N N N N N N N N N N N N N N N N
<del>187</del>	New Ho Ho Ho
203	

U.S. Scrial No.: 10/671,326

Page 27 of 53

***************************************	
204	HO NIN ON
205	HO THOM SOLVE TO THE SOLVE TO T
206	HO TON TON TON
207	Hose And
208	HO TO

U.S. Serial No.: 10/671,326 Page 28 of 53

209	HO COH
210	
210	HO CHING OF COMMENT OF
211	HO H
212	HO HO HO

U.S. Serial No.: 10/671,326

Page 29 of 53

213	HO,
214	HO WIND WILL ON O
215	MO M
216	HO THE STATE OF TH

U.S. Serial No.: 10/671,326

Page 30 of 53

217	10 x 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
218	
219	
220	HO TOH

U.S. Scrial No.: 10/671,326 Page 31 of 53

221	
222	
223	
224	HO JOH OH O
225	GI CI
226	HO NOT NOT NOT NOT NOT NOT NOT NOT NOT NO

U.S. Serial No.: 10/671,326 Page 32 of 53

227	
228	
229	MO HO
230	HO JOHHO N N OH
231	HO TOH HO NO OH

U.S. Serial No.: 10/671,326 Page 33 of 53

232	HO JOH OHHO N
233	HO, I, I, OH
234	HO JOH JIG JA JOH
235	

U.S. Serial No.: 10/671,326 Page 34 of 53

236	HO JOH HO N N N N N N N N N N N N N N N N N
237	HOO JOH OH HO NO OH OH
238	HO. TOHO OHIO NO. OHIO OHIO OHIO OHIO OHIO OHIO OHIO OH
239	HO JOH MO

U.S. Serial No.: 10/671,326

Page 35 of 53

240	HD CH NO
241	
242	
<del>243</del>	HO WHO OF THE OFFI
<del>2</del> 44	HO OH OH HO

U.S. Serial No.: 10/671,326

Page 36 of 53

<del>245</del>	N = M N
<del>246</del>	HO, HO OH OH
<del>247</del>	HO H
<del>248</del>	HO H
<del>249</del>	HO HO HO HO

U.S. Serial No.: 10/671,326 Page 37 of 53

<del>250</del>	HO OH
<del>251</del>	CI NON NON NON NON NON NON NON NON NON NO
<del>252</del>	P N N N N N N N N N N N N N N N N N N N
361	

U.S. Serial No.: 10/671,326

Page 38 of 53

362	
363	HO HO HO HOH
364	HO TON TON TON TON TON TON TON TON TON TO
365	HO TO

U.S. Serial No.: 10/671,326

Page 39 of 53

366	HO TO
367	CI NO ON
368	HO TO
369	HO. TOH

U.S. Serial No.: 10/671,326

Page 40 of 53

370	P
371	HO OH HO OH
372	HO OH HO OH
373	HO — N N N N N N N N N N N N N N N N N N

U.S. Serial No.: 10/671,326

Page 41 of 53

374	HO OH HO OH
375	HO H
376	HO TO
377	HO NEW NOTHON

U.S. Serial No.: 10/671,326

Page 42 of 53

378	HO NO
379	HO H
380	HO CH COH
381	HO 3

U.S. Serial No.: 10/671,326

Page 43 of 53

382	
383	
384	
385	HO OH OH
386	HO NO OH

U.S. Serial No.: 10/671,326 Page 44 of 53

387	HO I I ON
388	
389	HO TO HOLD TO
<del>390</del>	HOOOOOOOO .
<del>391</del>	HO H

. U.S. Serial No.: 10/671,326

Page 45 of 53

<del>392</del>	HO NON ON O
<del>393</del>	NO HO
<del>394</del>	HOOH
<del>395</del>	100
<del>396</del>	HO MAN O MI OH OH
<del>397</del>	HO O O O O O O O O O O O O O O O O O O

U.S. Serial No.: 10/671,326 Page 46 of 53

<del>398</del>	HO O
<del>399</del>	HQ O OH
<del>400</del>	HO OH OH
<del>401</del>	HOOH
4 <del>02</del>	HO with all the control of the contr

U.S. Serial No.: 10/671,326

Page 47 of 53

<del>403</del>	HO H
<del>404</del>	HO NO
<del>405</del>	HO H
<del>406</del>	

U.S. Serial No.: 10/671,326 Page 48 of 53

	·
<del>407</del>	
408	HO.
<del>409</del>	HO, HO
<del>410</del>	-N -O -N -N -O -N -N -O -N -N -O -N -N -O -N -N -O -N -N -O

U.S. Serial No.: 10/671,326

Page 49 of 53

411	CI — NO HO III — NOH O NOH
<del>412</del>	HO HO OH
4 <del>13</del>	HO H
414	HO TOH ON OH
415	

Amendment U.S. Serial No.:

U.S. Serial No.: 10/671,326 Page 50 of 53

or a pharmaceutically acceptable salt, ester, or prodrug thereof.

- 31. (Previously presented) A pharmaceutical composition comprising a compound according to claim 1 and a pharmaceutically acceptable carrier.
- 32. (Withdrawn) A method of treating a microbial infection in a mar smal comprising administering to the mammal an effective amount of a compound according to claim 1.
- 33.-38 (Cancelled)
- 39. (Withdrawn, Currently Amended) The method according to any one of claims 32-38 claim 32 wherein the compound is administered orally, parentally, or topically.
- 40.-42 (Cancelled) A method of synthesizing a compound according to claim 1.
- 43. (Previously presented) A pharmaceutical composition comprising a compound according to claim 30 and a pharmaceutically acceptable carrier.
- 44. (Cancelled)
- 45. (Previously presented) The compound according to claim 1, wherein G has the formula:

and R<sup>15</sup> is a macrolide.

Amendment U.S. Serial No.: 10/671,326 Page 51 of 53

- 46. (Previously presented) A pharmaceutical composition comprising a compound according to claim 18 and a pharmaceutically acceptable carrier.
- 47. (Previously presented) A pharmaceutical composition comprising a compound according to claim 19 and a pharmaceutically acceptable carrier.
- 48. (Cancelled)
- 49. (Previously presented) A pharmaceutical composition comprising a compound according to claim 45 and a pharmaceutically acceptable carrier.